Chemical Name: Afidopyropen
USEPA PC Code: 026200
USEPA MRID: 49689110
USEPA DP Barcode: 435146
PMRA Data Code (DACO): 9.2.3
PMRA Study No. (UKID): 2628087
Data Requirement: Non-guideline/OECD Guideline No. 207

Test Material: M440I005 (metabolite of BAS 440 I, Reg. No. 5824382) **Purity:** 90.9%

Active Ingredient: Afidopyropen
IUPAC Name: [(3*S*,4*R*,4a*R*,6*S*,6a*S*,12*R*,12a*S*,12b*S*)-3-(cyclopropylcarbonyloxy)-1,2,3,4,4a,5,6,6a,12a,12b-decahydro-6,12-dihydroxy-4,6a,12b-trimethyl-11-oxo-9-(3-pyridyl)-11*H*,12*H*-benzo[*f*]pyrano[4,3-*b*]chromen-4-yl]methylcyclopropane carboxylate
CAS Name: [(3*S*,4*R*,4a*R*,6*S*,6a*S*,12*R*,12a*S*,12b*S*)-3-(cyclopropylcarbonyl)oxy)]-1,3,4,4a,5,6,6a,12,12a,12b-decahydro-6,12-dihydroxy-4,6a,12b-trimethyl-11-oxo-9-(3-pyridyl)-2*H*,11*H*-naphtho[2,1-*b*]pyrano[3,4-*e*]pyran-4-yl]methyl cyclopropanecarboxylate
CAS No.: 915972-17-7
Synonyms: INSCALIS™

Primary Reviewer: Elizabeth A. Krupka
Environmental Scientist, CDM Smith/CSS-Dynamac JV
Signature:
Date: 30 December 2016

Secondary Reviewer: John Marton, Ph.D.
Environmental Scientist, CDM Smith/CSS-Dyanmac JV
Signature:
Date: 9 January 2017

USEPA Reviewer: Cameron Douglass, Ph.D.
Biologist, USEPA/OCSPP/OPP/EFED/ERBIV
Signature: 2018.02.16 14:31:22 -05'00'
Date: 16 February 2018

PMRA Reviewer: Vedad Izadi
Evaluation Officer, PMRA/EAD/ERSII
Date: 15 August 2017

Date Evaluation Completed: 15 August 2017

Note that the USEPA reviewer verified that statistical analyses (if appropriate) were correctly performed, but did not comprehensively revise the summary document prepared by CDM/CSS-Dynamac JV personnel ("the contractor"). The USEPA reviewer confirmed reported study author endpoints, but took at 'face value' the contractor's summary of the original study report.

CITATION:
Friedrich, S. 2014. Acute toxicity of Reg. No. 5824382 (Metabolite of BAS 440 I, M440I005) to the earthworm *Eisenia fetida* in artificial soil with 10 % peat. Study conducted and sponsored by BASF SE,

Ludwigshafen, Germany. BASF study code: 394883. Study initiated July 23, 2014 and completed October 30, 2014.

Executive Summary:
In a 14-day acute toxicity study, earthworms (*Eisenia fetida*) were exposed to metabolite M440I005 (purity 90.9%) of BAS 440 I at nominal concentrations of 0 (negative control), 62.5, 125, 250, 500, and 1000 mg/kg dry weight (dw) of soil (corresponding to concentrations of 0 (negative control), 56.8, 114, 227, 455, and 909 mg a.i./kg dw of soil when adjusting for purity of the test substance).

There was no mortality in the control or in any of the treatment groups. In the negative control, earthworm body weight decreased by an average of 5.3% mg. In the exposure groups, mean body weight decreases ranged from 4.9% to 5.9%. The differences in body weight were not significantly different relative to the control at any treatment level tested. No abnormal behavioral or toxic symptoms were observed in worms in the experimental treatment groups or control group during the test.

Earthworm mortality and growth were not affected by the test material, resulting in LC/EC_{50} and NOAEC values of >909 and 909 mg a.i./kg dw soil, respectively.

Results Synopsis:

Test Organism Size/Age (Mean Weight or Length): 330-528 mg/4 months old

LC/EC_{50}: >909 mg a.i./kg dw soil	95% C.I.: N/A
Probit Slope: N/A	95% C.I.: N/A
NOAEC: 909 mg a.i./kg dw soil	LOAEC: >909 mg a.i./kg dw soil

Endpoint(s) affected: None

EPA Classification: Supplemental (may be used quantitatively in risk estimation)
PMRA Classification: Fully reliable

I. DATA SOURCE

USEPA MRID No.:	49689110
PMRA UKID:	2628087
Study Title:	Acute toxicity of Reg. No. 5824382 (Metabolite of BAS 440 I, M440I005) to the earthworm *Eisenia fetida* in artificial soil with 10 % peat
Study Author(s):	Sabine Friedrich
Testing Laboratory:	BioChem agrar
Laboratory Report No.:	14 10 48 202 S
Sponsor Study No.:	394883
Study Completion Date:	October 30, 2014
Data Access:	Data submitter is data owner
Data Protection Claimed:	Yes

II. MATERIALS AND METHODS

Test Guideline: This study was conducted following guidelines outlined in OECD Guideline for Testing of Chemicals No. 207, “Earthworm, Acute Toxicity Test” (1984), and ISO-Guideline 11268-1:1993 “Soil

quality – Effects of pollutants on earthworms (Eisenia fetida) – Part 1: Determination of Acute Toxicity Using Artificial Soil Substrate. The reviewer assessed the study methods and results according to OECD 207 and to OCSPP 850.3100: Earthworm Subchronic Toxicity Test, even though OCSPP guidance is intended for chronic studies. The reviewer noted similarities and/or differences where they existed.

The following deviations from the OPPTS 850.3100 guidelines were noted:

Deviations from Guideline:

1. The earthworms were only acclimated for 1 day. The guidelines recommend at least 7 days of acclimation.
2. The study duration was only 14 days. The guidelines recommend 28 days.
3. The light intensity was 490 lux. This is in accordance with the OECD guidance range of 400 to 800 lux, while OPPTS guidance suggests a light intensity of ~420 lux.
4. The test material was mixed into the artificial soil before adding the earthworms. This is in accordance with OPPTS guidance, but OECD guidance suggests that the test material be sprayed on the soil surface after earthworms have been added and have burrowed into the soil.
5. The earthworms in the culture were fed with horse manure, which is in accordance with OECD guidance. OPPTS guidance suggests earthworms be fed commercial alfalfa pellets during culturing.
6. The total organic carbon content of the artificial soil was not reported. OPPTS guidance states that the TOC content of the soil should be determined at test initiation, while OECD guidance does not have the same requirement.
7. Test vessels were 1 liter and each replicate vessel contained 751 g wet weight (556 g dry weight) of soil. OCSPP guidance suggests test vessels of 1 pint in size, each containing 200 g dry weight of soil. OECD guidance suggests a test vessel with a volume of 1 liter, each containing 750 g wet weight of soil.
8. Test substance concentrations were not analytically verified.

GLP Compliance: Yes; study conducted in compliance with the OECD and German Principles of Good Laboratory Practice, which meet the U.S. EPA GLP standards (40 CFR Part 160 and 792), with the exception that recognized differences exist between the GLP principles/standards of OECD and those of the EPA.

A. MATERIALS

Test Material: Reg. No. 5824382, M440I005 (metabolite of BAS 440 I)

Test Material Identity: Batch no.: L82-73

Details on Preparation and Application of Test Materials:

For each treatment, weighed amounts of the test material (0.157, 0.313, 0.627, 1.254, and 2.508 g) were mixed with finely ground quartz such that 10 g of the mixture contained the required amount of the test substance for each replicate. The treated quartz sand was then added to 741 g wet weight of artificial soil, yielding 751 g wet artificial soil (corresponding to 556 g dry weight). The test item mixture was then mixed thoroughly with the artificial soil by intensive stirring in a laboratory mixer. The control contained quartz sand only and was left

	untreated. Each worm was washed, dried, and weighed prior to placement on the surface of the artificial treated soil.
Analytical Monitoring:	N/A; analytical verification was not performed
Details on Analytical Method:	N/A; analytical verification was not performed
Reference Material:	2-Chloroacetamide
Reference Material Identity	Not reported
Vehicle:	None
Test Organism (Species):	*Eisenia fetida* (earthworm)
Animal Group:	Phylum: Annelida; Class: Oligochaeta; Order: Haplotaxida; Family: Lumbricidae
Details on Test Organisms:	Clitellated adult earthworms approximately 4 months of age and 330 to 528 mg in weight. The earthworms were sourced from in-house cultures bred in a medium of horse manure, straw, peat (1:1:1).

B. STUDY DESIGN AND METHODS

Study Type:	Laboratory
Test Duration Type:	Acute
Limit Test:	No
Total Exposure Duration:	Exposure occurred at test initiation.
Post-Exposure Observation Period:	14 days
Remarks:	Standard methodologies
Test Environmental Conditions:	
	Temperature: 19.3 to 21.9°C Soil pH range at experimental start: 6.04 to 6.10 Soil pH range at experimental end: 5.85 to 5.91 Water content at experimental start: 35.0% Water content at experimental end: 34.3 to 34.6%
Photoperiod and Lighting:	Continuous illumination, supplied by Lumilux L58W, with a light intensity of 490 lux
Nominal Concentrations:	0 (negative control), 62.5, 125, 250, 500, and 1000 mg/kg dw of soil (corresponding to concentrations of 0 (negative control), 56.8, 114, 227, 455, and 909 mg a.i./kg dw of soil when adjusting for purity of the test substance).
Test Vessels:	1-liter glass containers covered with a glass lid allowing gas exchange, containing 751 g wet weight of the prepared material
Test Design:	Adult earthworms were exposed to the test substance by placing them on the surface of treated soil. Four replicate test containers were maintained for each test group, consisting of 10 earthworms. Behavior was assessed immediately after exposure, and after 7 and 14 days of treatment. Mortality was also assessed at 7 and 14 days after treatment. Body weight change was assessed 14 days after treatment.

III. APPLICANT'S REPORTED RESULTS AND DISCUSSION

Exposure Duration: 14 days
Endpoint(s): Mortality; Body weight change
Effect Concentration: LC_{50}: >1000 mg/kg dw; NOAEC: 1000 mg/kg dw
Basis for Concentration: Nominal
Effect Concentration Type: Test material
Basis for Effect: Mortality

Details on Applicant-Provided Results:
There was no mortality in the control or in any of the treatment groups. In the negative control, earthworm body weight decreased by an average of 20.8 mg wet weight (range of 14.50 mg to 28.20 mg per replicate). In the exposure groups, mean body weight decreases ranged from 19.40 to 23.28 mg (range of 11.70 to 33.60 mg per replicate). No abnormal behavioral or toxic symptoms were observed in worms in the experimental treatment groups or control group during the test.

Table 1: Study-author reported effect of M440I005 (a transformation product of BAS 440 I, afidopyropen) on mortality of *Eisenia fetida*.

Nominal concentration (mg/kg soil)	Observation period			
	Day 7		Day 14	
	No. Dead	% Mortality	No. Dead	% Mortality
Control	0	0	0	0
62.5	0	0	0	0
125	0	0	0	0
250	0	0	0	0
500	0	0	0	0
1000	0	0	0	0
LC_{50}	>1000 mg/kg soil dry weight (based on nominal concentrations)			

Table 2: Study-author reported effects of M440I005 (a transformation product of BAS 440 I, afidopyropen) on growth of *Eisenia fetida*.

Nominal concentration (mg/kg soil)	Observation period			
	Day 0		Day 14	
	Weight (mg/worm)	% Loss	Weight (mg/worm)	% Loss
Control	391.6	N/A	370.8	-20.8
198	392.2	N/A	372.8	-19.4
296	393.9	N/A	373.5	-20.4
444	393.0	N/A	371.5	-21.5
667	391.1	N/A	370.9	-20.2
1000	391.5	N/A	368.3	-23.3
IC_{50}	N/A			

Applicant-Reported Statistics and Error Estimates

The test data was analyzed with the software ToxRat Professional 2.10.06 (Ratte 2010). The Williams-t-test was used to compare the control with the independent test item groups. Due to <50% mortality the LC_{50} was estimated to be >1,000 mg/kg soil dry weight. The NOAEC was determined to be 1,000 mg/kg soil dry weight.

IV. OVERALL REMARKS, ATTACHMENTS

The applicant submitted a full study report (PDF document), and an OECD-formatted summary document.

V. PRIMARY REVIEWER'S ANALYSIS AND CONCLUSIONS

Reviewer's Statistical Verification:

The reviewer entered the mortality and % body weight change data into CETIS statistical software version 1.8.7.12 with database backend settings implemented by EFED on 10/20/15. Analyses were conducted using the nominal test concentrations. There was no mortality or other significant treatment effects in this study, so LC/EC_{50} values and NOAEC values were qualitatively estimated relative to the highest tested concentration (*i.e.*, no statistical analyses were conducted and no reports are attached).

LC/EC_{50}: >909 mg a.i./kg dw soil	95% C.I.: N/A
Probit Slope: N/A	95% C.I.: N/A
NOAEC: 909 mg a.i./kg dw soil	LOAEC: >909 mg a.i./kg dw soil

Reviewer's Comments:

The reviewer adjusted nominal concentrations based on the purity of the test material (90.9%); the study author reported results using the unadjusted nominal concentrations. The reviewer's results and the study author's results were in agreement; there was no treatment-related toxicity in this study.

The in-life phase of the study was conducted from August 6 to August 20, 2014.

Reviewer's Conclusions:

There were no treatment-related effects of Reg. No. 5824382 (Metabolite of BAS 440 I, M440I005) on earthworms for any endpoint tested. The LC/EC_{50} were >909 mg a.i./kg soil.

Results Synopsis:

Test Organism Size/Age (Mean Weight or Length): 330-528 mg/4 months old

LC/EC_{50}: >909 mg a.i./kg dw soil	95% C.I.: N/A
Probit Slope: N/A	95% C.I.: N/A
NOAEC: 909 mg a.i./kg dw soil	LOAEC: >909 mg a.i./kg dw soil

Endpoint(s) affected: None

EPA Classification: Supplemental (may be used quantitatively in risk estimation)
PMRA Classification: Fully reliable

OCSPP 850.3100 Earthworm Subchronic Toxicity Test **IBACON**

Batch ID:	02-1314-3287	**Test Type:**	Subchronic Earthworm Toxicity	**Analyst:**	
Start Date:	01 Aug-14	**Protocol:**	OECD 207: Acute Earthworm Toxicity	**Diluent:**	Deionized Water
Ending Date:		**Species:**	Eisenia fetida	**Brine:**	
Duration:	NA	**Source:**	IBACON GmbH	**Age:**	
Sample ID:	10-0311-7658	**Code:**	49689109	**Client:**	CDM Smith - E. Krupka
Sample Date:	01 Aug-14	**Material:**	M4401003 (Afidopyropen metabolite)	**Project:**	Insecticide
Receive Date:		**Source:**	BASF SE		
Sample Age:	NA	**Station:**			

Batch Note: MRID 49689109
Sample Note: MRID 49689109

Comparison Summary

Analysis ID	Endpoint	NOEL	LOEL	TOEL	PMSD	TU	Method
08-9604-1292	14dMortalityRate	1000	>1000	NA	2.8%		Mann-Whitney U Two-Sample Test

14dMortalityRate Summary

C-mg/kg soil	Control Type	Count	Mean	95% LCL	95% UCL	Min	Max	Std Err	Std Dev	CV%	%Effect
0	Negative Control	4	0	0	0	0	0	0	0		
62.5		4	0	0	0	0	0	0	0		
125		4	0	0	0	0	0	0	0		
250		4	0	0	0	0	0	0	0		
500		4	0.025	0	0.105	0	0.1	0.025	0.05	200.0%	
1000		4	0	0	0	0	0	0	0		

14dMortalityRate Detail

C-mg/kg soil	Control Type	Rep 1	Rep 2	Rep 3	Rep 4
0	Negative Control	0	0	0	0
62.5		0	0	0	0
125		0	0	0	0
250		0	0	0	0
500		0	0.1	0	0
1000		0	0	0	0

OCSPP 850.3100 Earthworm Subchronic Toxicity Test **IBACON**

Analysis ID:	08-9604-1292	**Endpoint:**	14dMortalityRate	**CETIS Version:**	CETISv1.8.7
Analyzed:	03 Jan-17 22:06	**Analysis:**	Nonparametric-Two Sample	**Official Results:**	Yes
Batch ID:	02-1314-3287	**Test Type:**	Subchronic Earthworm Toxicity	**Analyst:**	
Start Date:	01 Aug-14	**Protocol:**	OECD 207: Acute Earthworm Toxicity	**Diluent:**	Deionized Water
Ending Date:		**Species:**	Eisenia fetida	**Brine:**	
Duration:	NA	**Source:**	IBACON GmbH	**Age:**	

Data Transform	Zeta	Alt Hyp	Trials	Seed	PMSD	NOEL	LOEL	TOEL	TU
Untransformed	NA	C > T	NA	NA	2.8%	1000	>1000	NA	

Mann-Whitney U Two-Sample Test

Control	vs	C-mg/kg soil	Test Stat	Critical	Ties	DF	P-Value	P-Type	Decision(α:5%)
Negative Control		62.5	8	NA	1	6	1.0000	Exact	Non-Significant Effect
		125	8	NA	1	6	1.0000	Exact	Non-Significant Effect
		250	8	NA	1	6	1.0000	Exact	Non-Significant Effect
		500	6	NA	1	6	1.0000	Exact	Non-Significant Effect
		1000	8	NA	1	6	1.0000	Exact	Non-Significant Effect

ANOVA Table

Source	Sum Squares	Mean Square	DF	F Stat	P-Value	Decision(α:5%)
Between	0.002083333	0.0004166667	5	1	0.4457	Non-Significant Effect
Error	0.0075	0.0004166667	18			
Total	0.009583334		23			

Distributional Tests

Attribute	Test	Test Stat	Critical	P-Value	Decision(α:1%)
Variances	Mod Levene Equality of Variance	1	4.25	0.4457	Equal Variances
Variances	Levene Equality of Variance	9	4.25	0.0002	Unequal Variances
Distribution	Shapiro-Wilk W Normality	0.463	0.884	<0.0001	Non-normal Distribution

14dMortalityRate Summary

C-mg/kg soil	Control Type	Count	Mean	95% LCL	95% UCL	Median	Min	Max	Std Err	CV%	%Effect
0	Negative Control	4	0	0	0	0	0	0	0		
62.5		4	0	0	0	0	0	0	0		
125		4	0	0	0	0	0	0	0		
250		4	0	0	0	0	0	0	0		
500		4	0.025	0	0.105	0	0	0.1	0.025	200.0%	
1000		4	0	0	0	0	0	0	0		

Graphics